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(54) Title: TOPICAL RETINOID COMPOSITION

(57) Abstract

Disclosed are topical retinol compositions and methods of applying such compositions to human skin. The topical compositions comprise (a) from about 1 % to about 60 % of a continuous silicone phase by weight of the composition, wherein the continuous silicone phase comprises from about 50 % to about 99.9 % organopolysiloxane and less than about 50 % by weight of a nonsilicone oil, by weight of the continuous silicone phase; (b) from about 30 % to about 90 % of an aqueous discontinuous phase by weight of the composition; (c) from about 0.0001 % to about 5 % retinoid by weight of the composition; and (d) from about 0.1 % to about 10 % of an emulsifier by weight of the composition. The topical compositions provide improved oxidative stability for retinoids incorporated in water-in-oil emulsions, and are preferably substantially free of conventional antioxidants.

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TOPICAL RETINOID COMPOSITION

TECHNICAL FIELD

The present invention relates to topical retinoid compositions in the form of water-in-silicone emulsions that provide improved oxidative stability for the retinoid therein.

BACKGROUND OF THE INVENTION

Various retinoid compositions are known for topical use on human skin. These topical retinoids can improve the texture or appearance of skin, especially aged or wrinkled skin, or skin that has been excessively exposed to ultraviolet radiation, wind, low humidity, harsh surfactants, abrasives, and the like. Retinoids most commonly described for this purpose include retinol, retinal, retinoic acid, and retinyl esters, which can be incorporated into and applied as aqueous gels, anhydrous ointments or creams, water-in-oil emulsions or oil-in-water emulsions.

Water-in-oil emulsions are especially useful vehicles for moisturizing and delivering active materials such as retinoids to the skin. When applied to the skin, the discontinuous water phase provides moisture to the skin under an occlusive oil layer provided by the continuous oil phase of the emulsion. The oil soluble retinoids are typically contained in the oil phase, and after topical application, diffuse through the applied oil layer to the surface of the skin. However, many of these water-in-oil emulsion compositions are oxidatively unstable, due primarily to trace contaminants in the water and oil materials used in formulating the emulsion, and cannot be stored for more than a
brief period of time without undesirable oxidation of the retinoid. Retinol is especially susceptible to oxidation in these water-in-oil emulsion systems.

Water-in-silicone emulsions are especially useful in providing a means for topically delivering active materials to the skin. These silicone-based emulsions normally provide easier spreadability, lower occlusion, and contain higher water concentrations for skin moisturization than comparable non-silicone based water-in-oil emulsions. However, the oxygen permeability of the silicone oil in these emulsions is normally greater than for most nonsilicon oils, thus reducing oxidativ stability of any oxidative-sensitive materials therein.

One attempt at improving the oxidative stability of retinoid-containing water-in-oil emulsions involves the us of antioxidants in combination with the r tinoid. These antioxidants are especially useful when used in combination with highly oxidation-sensitive retinoids such as retinol. Although antioxidants would seem to improve oxidative stability of certain retinoids in these emulsion systems, and even permit the use of retinol in a water-in-silicone emulsion system, these added materials can increase raw material costs and introduce additional chemical and physical compatibility issues.

It has now been found that select water-in-silicone emulsion systems can be formulated to provide an oxidatively stable vehicle for topical retinoids. The select emulsion systems comprise a discontinuous aqueous phase dispersed in a continuous silicone phase, wherein the continuous silicone phase comprises between about 50% and about 99.9% by weight of organopolysiloxane oil and less than about 50% by weight of a non-silicone oil. It has been found that the polyorganosiloxane oil component, when incorporated into the water-in-silicone emulsion system described herein, provides topical retinoids with more oxidative stability over extended periods of time than comparable water-in-oil emulsions containing lower concentrations of the polyorganosiloxane oil. This finding was especially unexpected in view of the prior art which teaches that silicone oils have higher oxygen permeabilities than other non-silicone oils, and that higher oxygen permeabilities will enhance rather than reduce oxidative processes therein.

It is therefore an object of the present invention to provide a novel retinoid composition suitable for topical application on human skin, and further to provide such a composition that provides moisturization and topical delivery of a retinoid, and further to provide such a composition that is in the form of a water-in-silicone emulsion which provides improved oxidative stability for the retinoid therein.

SUMMARY OF THE INVENTION

The present invention is directed to topical compositions comprising (a) from about 1% to about 60% of a continuous silicone phase by weight of the composition, wherein the continuous silicone phase comprises (i) from about 50% to about 99.9% organopolysiloxan and less than about 50% by weight of a nonsilicone oil, by weight of th continuous silicon phase; (b)

from about 30% to about 90% of an aqueous discontinuous phase by weight of the composition; (c) from about 0.0001% to about 5% retinoid by weight of the composition; and (d) from about 0.1% to about 10% of an emulsifier by weight of the composition. The topical compositions provide improved oxidative stability for retinoids in water-in-silicone emulsions, and are preferably substantially free of added antioxidant materials. The present invention is also directed to methods of using the topical compositions on human skin.

DETAILED DESCRIPTION OF THE INVENTION

The topical compositions of the present invention are water-in-silicone emulsions which comprise a discontinuous aqueous phase, a continuous silicone phase, a retinoid dispersed or dissolved in the continuous silicone phase, and an emulsifier. Each of these essential components are described in detail hereinafter.

The compositions of the present invention are useful for topical application on human skin to deliver a safe and effective amount of a retinoid to the skin. In this context, the phrase "safe and effective" refers to an amount of retinoid in the composition that when topically applied will improve the appearance and/or texture of human skin, but will avoid serious side effects, e.g, to provide a reasonable benefit to risk ratio within the scope of sound medical judgment. The skilled artisan will appreciate that topical retinoids can help minimize or eliminate the development of wrinkles, including both fine superficial wrinkles and coarse deep wrinkles, skin lines, sagging, discoloration, age spots, keratoses, hyperkeratinization, elastosis, collagen breakdown, and/or other histological changes in the stratum corneum, dermis, epidermis, the vascular system, and underlying tissues.

A key characteristic of the compositions of the present invention is that they remain surprisingly stable over an extended period of time, especially when packaged and stored for periods of time exceeding about sixty days. In this context, the term "stable" refers to improved oxidative stability of the dispersed retinoid in the continuous silicone phase of the composition. As a result of this improved oxidative stability, the compositions may be packaged and stored as commercial product for extended periods, even though such compositions may be substantially free of antioxidants.

All parts, p rcentag s and ratios as us d herein ar by w ight of th total composition and all measurements are made at 25°C, unless otherwis

specified. All weight percentages are on an actives weight basis, unless otherwise specified.

The compositions of the present invention can comprise, consist of, or consist essentially of, the essential as well as optional ingredients, components, or limitations described in detail hereinafter.

Retinoid

The continuous silicone phase of the compositions of the present invention comprise a safe and effective amount of a retinoid, preferably at concentrations of from about 0.0001% to about 5%, preferably from about 0.01% to about 2%, more preferably from about 0.01% to about 1%, by weight of the compositions.

Suitable retinoids include retinol, synthetic or natural analogs of retinol, and geometric and stereoisomers of such compounds. Preferred retinoids include retinol, retinoic acid, retinal and retinyl esters such as retinyl acetate, retinyl butyrate, retinyl propionate, retinyl octanoate, retinyl laurate, retinyl palmitate, retinyl oleate and retinyl linoleate. Most preferred are those retinoids that are highly suseptable to oxidation in a water-in-oil emulsion, e.g., retinol.

Continuous Silicone Phase

The topical compositions of the present invention comprise from about 1% to about 60%, preferably from about 5% to about 40%, more preferably from about 10% to about 20%, by weight of a continuous silicone phase, wherein the continuous silicone phase comprises at least about 50%, preferably from about 60% to about 99.9%, more preferably from about 70% to about 99.9%, and even more preferably from about 80% to about 99.9%, polyorganosiloxane oil by weight of the continuous silicone phase.

The continuous oil phase of the composition herein may comprise up to about 50% non-silicone oils, preferably less about 40%, more preferably less than about 30%, even more preferably less than about 10%, and most preferably less than about 2%, by weight of the continuous silicone phase. Concentrations of non-silicone oils in the continuous silicone phase are minimized so as to further enhance oxidative stability of the selected retinoid in the compositions. It has been found that retinoids, especially retinol, are less susceptible to oxidation when incorporated into water-in-oil systems containing at least 50% by weight of organopolysiloxan oil, than in

comparabl systems containing lower or no concentrations of organopolysiloxane oil..

The organopolysiloxan oil for use in the composition may be volatile, non-volatile, or a mixture of volatile and non-volatile silicones. The term "nonvolatile" as used in this context refers to those silicones that are liquid under ambient conditions and have a flash point (under one atmospheric of pressure) of at greater than about 100°C. The term "volatile" as used in this context refers to all other silicone oils.

The phrase "continuous silicone phase" as used herein refers to the continuous oil phase of the composition, which oil phase comprises at least about 50% by weight of polyorganosiloxane oil, and exists as an external phase that contains or surrounds the discontinuous aqueous phase described hereinafter. The "oil" referred to herein has a melting point of about 25°C or less under about one atmosphere of pressure.

Suitable organopolysiloxanes can be selected from a wide variety of silicones spanning a broad range of volatilities and viscosities. Examples of suitable organopolysiloxane oils include polyalkylsiloxanes, cyclic polyalkylsiloxanes, and polyalkylarylsiloxanes. Polyalkylsiloxanes useful in the composition herein include polyalkylsiloxanes with viscosities of from about 0.5 to about 1,000,000 centistokes at 25°C. Such polyalkylsiloxanes can be represented by the general chemical formula $R_3SiO[R_2SiO]_xSiR_3$ wherein R is an alkyl group having from one to about 30 carbon atoms (preferably R is methyl or ethyl, more preferably methyl; also mixed alkyl groups can be used in the same molecule), and x is an integer from 0 to about 10,000, chosen to achieve the desired molecular weight which can range to over about 10,000,000. Commercially available polyalkylsiloxanes include the polydimethylsiloxanes, which are also known as dimethicones, examples of which include the Vicasil® series sold by General Electric Company and the Dow Corning® 200 series sold by Dow Corning Corporation. Specific examples of suitable polydimethylsiloxanes include Dow Corning® 200 fluid having a viscosity of 0.65 centistokes and a boiling point of 100°C, Dow Corning® 225 fluid having a viscosity of 10 centistokes and a boiling point greater than 200°C, and Dow Corning® 200 fluids having viscosities of 50, 350, and 12,500 centistokes, respectively, and boiling points greater than 200°C. Suitable dimethicones include those represent d by the chemical formula $(CH_3)_3SiO[(CH_3)_2SiO]_x[CH_3RSiO]_ySi(CH_3)_3$ wherein R is straight or

branched chain alkyl having from two to about 30 carbon atoms and x and y are each integers of 1 or greater selected to achieve the desir d molecular weight which can range to over about 10,000,000. Examples of these alkyl-substituted dimethicones include cetyl dimethicone and lauryl dimethicone.

Cyclic polyalkylsiloxanes suitable for use in the composition include those represented by the chemical formula $[SiR_2-O]_n$ wherein R is an alkyl group (preferably R is methyl or ethyl, more preferably methyl) and n is an integer from about 3 to about 8, more preferably n is an integer from about 3 to about 7, and most preferably n is an integer from about 4 to about 6. When R is methyl, these materials are typically referred to as cyclomethicones. Commercially available cyclomethicones include Dow Corning® 244 fluid having a viscosity of 2.5 centistokes, and a boiling point of 172°C, which primarily contains the cyclomethicone tetramer (i.e. n=4), Dow Corning® 344 fluid having a viscosity of 2.5 centistokes and a boiling point of 178°C, which primarily contains the cyclomethicone pentamer (i.e. n=5), Dow Corning® 245 fluid having a viscosity of 4.2 centistokes and a boiling point of 205°C, which primarily contains a mixture of the cyclomethicone tetramer and pentamer (i.e. n=4 and 5), and Dow Corning® 345 fluid having a viscosity of 4.5 centistokes and a boiling point of 217°, which primarily contains a mixture of the cyclomethicone tetramer, pentamer, and hexamer (i.e. n=4, 5, and 6). Also useful are materials such as trimethylsiloxysilicate, which is a polymeric material corresponding to the general chemical formula $[(CH_2)_3SiO_{1/2}]_x[SiO_2]y$, wherein x is an integer from about 1 to about 500 and y is an integer from about 1 to about 500. A commercially available trimethylsiloxysilicate is sold as a mixture with dimethicone as Dow Corning® 593 fluid.

Dimethiconols are also suitable for use in the composition. These compounds can be represented by the chemical formulas $R_3SiO[R_2SiO]_xSiR_2OH$ and $HOR_2SiO[R_2SiO]_xSiR_2OH$ wherein R is an alkyl group (preferably R is methyl or ethyl, more preferably methyl) and x is an integer from 0 to about 500, chosen to achieve the desired molecular weight. Commercially available dimethiconols are typically sold as mixtures with dimethicone or cyclomethicone (e.g. Dow Corning® 1401, 1402, and 1403 fluids).

Polyalkylaryl siloxanes are also suitable for use in the composition. Polymethylphenyl siloxanes having viscositi s from about 15 to about 65 centistokes at 25°C are specially useful.

As stated hereinbefore, the continuous silicone phase comprises less than about 50% by weight of a non-silicone oil by weight of th continuous silicone phase, and preferably the concentration of such non-silicone oils is minimized or avoided altogether in formulating the continuous silicone oil phase of the compositions herein. Examples of non-silicone oils suitable for use in the continuous silicone phase, and which are preferably minimized or avoided in the compositions herein, are well known in the chemical arts in topical personal care products in the form of water-in-oil emulsions, e.g., mineral oil, vegetable oils, synthetic oils, semisynthetic oils, etc.

Discontinuous Aqueous Phase

The topical compositions of the present invention comprise from about 30% to about 90%, more preferably from about 50% to about 85%, and most preferably from about 70% to about 80% of a discontinuous aqueous phase. The discontinuous aqueous phase is a dispersion of small aqueous particles or droplets suspended in and surrounded by the continuous silicone phase described hereinbefore.

The discontinuous aqueous phase can be water, or a combination of water and one or more water soluble or dispersible ingredients. Examples of such option ingredients include thickeners, acids, bases, salts, chelants, gums, water-soluble or dispersible alcohols and polyols, buffers, preservatives, sunscreening agents, colorings, and the like.

The topical compositions of the present invention will typically comprise from about 25% to about 90%, preferably from about 40% to about 80%, more preferably from about 60% to about 80%, water in the discontinuous aqueous phase by weight of the composition.

Emulsifier

The topical compositions of the present invention comprise from about 0.1% to about 10%, preferably from about 0.5% to about 7.5%, more preferably from about 1% to about 5% , emulsifier by weight of the composition. The emulsifier helps disperse and suspend the discontinuous aqueous phase within the continuous silicone phase of the composition.

Known or conventional emulsifying agents can be used in the composition, provided that the selected emulsifying agent is chemically and physically compatible with essential compon nts of th composition, and provides the desired dispersion characteristics. Suitable emulsifiers include

silicone emulsifiers, non-silicon-containing emulsifiers, and mixtures thereof, known by those skilled in the art for use in topical personal care products. Preferably these emulsifiers have an HLB value of less than about 14, more preferably from about 2 to about 14, and most preferably from about 4 to about 14. Emulsifiers having an HLB value outside of these ranges can be used in combination with other emulsifiers to achieve an effective weighted average HLB for the combination that falls within the ranges described herein.

Silicone emulsifiers are preferred in the compositions herein. These emulsifiers are typically organically modified organopolysiloxanes, also known as silicone surfactants. Especially useful silicone emulsifiers include dimethicone copolyols, which are polydimethyl siloxanes which have been modified to include polyether side chains such as polyethylene oxide chains, polypropylene oxide chains, mixtures of these chains, and polyether chains containing moieties derived from both ethylene oxide and propylene oxide. Other examples include alkyl-modified dimethicone copolyols, i.e. compounds which contain pendent C2-C30 pendant side chains. Still other useful dimethicone copolyols include materials having various cationic, anionic, amphoteric, and zwiterionic pendant moieties.

Dimethicone copolyol emulsifiers useful in the composition herein are described, for example, in U.S. Patent No. 4,960,764; EP 330,369; G.H. Dahms, et al., "New Formulation Possibilities Offered by Silicone Copolyols," *Cosmetics & Toiletries*, vol. 110, pp. 91-100, March 1995; M.E. Carlotti et al., "Optimization of W/O-S Emulsions And Study Of The Quantitative Relationships Between Ester Structure And Emulsion Properties," *J. Dispersion Science And Technology*, 13(3), 315-336 (1992); P. Hameyer, "Comparative Technological Investigations of Organic and Organosilicone Emulsifiers in Cosmetic Water-in-Oil Emulsion Preparations," *HAPPI* 28(4), pp. 88-128 (1991); J. Smid-Korbar et al., "Efficiency and useability of silicone surfactants in emulsions," *Provisional Communication, International Journal of Cosmetic Science*, 12, 135-139 (1990); and D.G. Krzysik et al., "A New Silicone Emulsifier For Water-in-Oil Systems," *Drug and Cosmetic Industry*, vol. 146(4) pp. 28-81 (April 1990); which descriptions are incorporated herein by reference.

Suitable non-silicone emulsifiers include various non-ionic and anionic emulsifying agents such as sugar esters and polyesters, alkoxylated sugar esters and polyesters, C1-C30 fatty acid esters of C1-C30 fatty alcohols,

alkoxylated derivatives of C1-C30 fatty acid esters of C1-C30 fatty alcohols, alkoxylated ethers of C1-C30 fatty alcohols, polyglyceryl esters of C1-C30 fatty acids, C1-C30 esters of polyols, C1-C30 ethers of polyols, alkyl phosphates, polyoxyalkylene fatty ether phosphates, fatty acid amides, acyl lactylates, soaps, and mixtures thereof.

Other suitable emulsifiers are described, for example, in McCutcheon's, Detergents and Emulsifiers, North American Edition (1986), published by Allured Publishing Corporation; U.S. Patent 5,011,681; U.S. Patent 4,421,769; and U.S. Patent 3,755,560, which descriptions are incorporated herein by reference.

Optional Materials

The topical composition of the present invention may further comprise one or more optional components, provide that such optional components are chemically and physically compatible with the essential components of the composition, or do not unduly affect product performance.

The topical compositions are preferably substantially free of conventional antioxidants which are known for use in improving oxidative stability of susceptible materials in personal care products. Although it is understood that the topical compositions may optionally contain such conventional antioxidants. Examples of antioxidants include butylated hydroxytoluene, butylated hydroxyanisole, ascorbic acid, propyl gallate, and alpha tocopherol, and examples of chelants include ethylenediaminetetracetic acid (EDTA) and related materials. The phrase "substantially fee" as used herein refers to concentrations of antioxidant in the water-in-silicone compositions of the present invention that are too low to significantly improve oxidative stability of the selected retinoid in the compositions herein.

Optional materials include sunscreening agents, examples of which a described in U.S. Patent 5,087,445; U.S. Patent 5,073,372; U.S. Patent 5,073,371; and Segarin, et al., at Chapter VIII, pages 189 et seq., of Cosmetics Science and Technology, which descriptions are incorporated herein by reference. Other optional materials include sunless tanning agents, and skin bleaching or lightening agents.

Oth r optional materials include known or conventional humectant, moisturizing, or skin conditioning materials. Concentrations of such opti nal

materials will generally range from about 0.1% to about 20%, preferably from about 1% to about 10%, most preferably from about 2% to about 5%, by weight of the composition. These materials include guanidine; glycolic acid and glycolate salts; lactic acid and lactate salts; aloe vera; polyhydroxy alcohols; polyethylene glycols; sugars and starches; sugar and starch derivatives; hyaluronic acid; lactamide monoethanolamine; acetamide monoethanolamine; propoxylated glycerols, C1-C30 monoesters and polyesters of sugars and related materials, and mixtures thereof.

Other optional materials include cosmetic and pharmaceutical ingredients commonly used in the skin care industry, examples of which include absorbents, abrasives, anti-acne agents, anticaking agents, antifoaming agents, antimicrobial agents, binders, biological additives, buffering agents, bulking agents, chemical additives, colorants, cosmetic astringents, cosmetic biocides, denaturants, drug astringents, external analgesics, film formers, fragrance components, humectants, opacifying agents, pH adjusters, plasticizers, preservatives, propellants, reducing agents, additional skin-conditioning agents, skin protectants, solvents, suspending agents (nonsurfactant), ultraviolet light absorbers, viscosity increasing agents (aqueous and nonaqueous) and solubilizing agents. These and other optional materials are described, for example, in The CTFA Cosmetic Ingredient Handbook, Second Edition, 1992, which is incorporated herein by reference in its entirety.

The composition of the present invention may further comprise additional materials known for use in topical compositions to improve the appearance and/or texture of aged or otherwise wrinkled skin. Examples of such optional materials include N-acetylcysteine, N-acetyl-L-cysteine, N-acetyl-D-cysteine, derivatives thereof and salts thereof, descriptions of which are set forth in U.S. Patent 5,296,500, which descriptions are incorporated herein by reference. Concentrations of N-acetylcysteine and related compounds will generally range from about 0.01% to about 50%, preferably from about 0.1% to about 10%, more preferabbly from about 0.25% to about 5%, by weight of the composition.

Other optional materials include aesthetic components such as fragrances, pigments, colorings, essential oils, skin sensates, astringents, skin soothing agents and skin healing agents.

Methods of Use

The compositions of the present invention may be applied topically to human skin to improve the appearance and/or texture of the skin, or to otherwise deliver topical retinoids to human skin. In particular, the compositions of the present invention may be topically applied to human skin to help reduce, efface, and/or prevent wrinkles in human skin, to help moisturize skin, and to help treat histological changes associated with skin aging or excessive exposure to ultraviolet radiation, wind, low humidity, harsh surfactants, and/or abrasives.

Methods of using the composition comprise applying to the skin a safe and effective amount of the compositions of the present invention. The amount of the retinoid in the composition and the frequency of application on the skin will vary widely depending upon the condition of the skin and the effect desired. Such methods will typically involve application of from about 0.1 mg/cm^2 to about 10 mg/cm^2 (mg of the composition per area of skin).

EXAMPLES

The following nonlimiting examples illustrate specific embodiments of the topical compositions of the present invention, including methods of manufacture and use.

EXAMPLE 1

The following describes a retinol-containing water-in-silicone emulsion of the present invention. The composition is prepared by combining the following ingredients using conventional mixing techniques.

Ingredient	weight %
Water	qs 100
Cyclomethicone[1]	15.0
Ethanol	3.0
Glycerin	3.0
Polyglyceryl-4 Isostearate (and) Cetyl Dimethicone Copolyol (and) Hexyl Laurate[2]	2.50
Cyclomethicone (and) Dimethicon Copolyol[3]	2.50
Tetrasodium EDTA	0.50

Benzyl Alcohol	0.30
Methyl Paraben	0.20
Fragrance	0.20
Retinol [4]	0.10

[1] Dow Corning® 345 fluid from Dow Corning.
[2] Abil WE-09 from Goldschmidt.
[3] Dow Corning® 3225C from Dow Corning
[4] Vitamin A alcohol blend from Roche Vitamins and Fine Chemicals

In a suitable vessel the methyl paraben, benzyl alcohol and ethanol are combined with mixing until a solution is obtained. Next, the water, glycerin, and tetrasodium EDTA are added with mixing. In a separate vessel, Vitamin A alcohol , cyclomethicone, polyglyceryl-4 isostearate (and) cetyl dimethicone copolyol (and) hexyl laurate, and cyclomethicone (and) dimethicone copolyol are first combined and then added with mixing to form the emulsion. Next the fragrance is added with stirring.

The resulting water-in-silicone composition is useful for application of retinol to human skin, and to improving the appearance and texture of human skin. The resulting composition provides oxidative stability for the retinol.

EXAMPLE 2

The following describes a retinoid-containing water-in-silicone emulsion of the present invention. The retinoid is retinyl palmitate. The composition is prepared by combining the following ingredients using conventional mixing techniques.

Ingredient	weight %
Water	qs 100
Cyclomethicone[1]	15.0
Ethanol	3.0
Glycerin	3.0
Polyglyceryl-4 Isostearate (and) Cetyl Dimethicone Copolyol (and) Hexyl Laurate[2]	2.50
Cyclomethicone (and)	

Dimethicone Copolyol[3]	2.50
Tetrasodium EDTA	0.50
Benzyl Alcohol	0.30
Methyl Paraben	0.20
Fragrance	0.20
Retinyl palmitate [5]	0.10

[5] Vitamin A Palmitate from Roche Vitamins and Fine Chemicals

In a suitable vessel the methyl paraben, benzyl alcohol and ethanol are combined with mixing until a solution is obtained. Next, the water, glycerin, and tetrasodium EDTA are added with mixing. In a separate vessel, Vitamin A palmitate, cyclomethicone, polyglyceryl-4 isostearate (and) cetyl dimethicone copolyol (and) hexyl laurate, and cyclomethicone (and) dimethicone copolyol are first combined and then added with mixing to form the emulsion. Next the fragrance is added with stirring.

The resulting water-in-silicone composition is useful for application of a retinoid to human skin, and to improving the appearance and texture of human skin. The resulting composition provides oxidative stability for the retinoid.

What is claimed is:

1. A topical composition comprising:
(a) from 1% to 60% of a continuous silicone phase by weight of the composition, wherein the continuous silicone phase comprises
(i) from 50% to 99.9% organopolysiloxane by weight of the continuous silicone phase, and
(ii) less than 50% nonsilicone oil by weight of the continuous silicone phase;
(b) from 30% to 90% of an aqueous discontinuous phase by weight of the composition;
(c) from 0.0001% to 5% retinoid by weight of the composition; and
(d) from 0.1% to 10% of an emulsifier, preferably a silicone emulsifier, by weight of the composition.

2. The composition of Claim 1 wherein the continuous silicone phase comprises from 60% to 99.9%, preferably from 90% to 99.9%, organopolysiloxane and less than 40%, preferably less than 10%, by weight of nonsilicone oils, by weight of the continuos silicone phase.

3. The composition of any one of the preceding claims wherein the retinoid is selected from the group consisting of retinol, retinal, retinoic acid, esters thereof and combinations thereof, preferably retinol.

4. The composition of any one of the preceding claims further comprising a material selected from the group consisting of N-acetylcysteine, N-acetyl-L-cysteine, N-acetyl-D-cysteine, derivatives thereof, salts thereof and combinations thereof.

5. The composition of any one of the preceding claims wherein the composition is substantially free of antioxidants.

6. A method for topically applying retinoids to human skin, which method comprises topically applying to the skin a safe and effective amount of the composition of any one of the preceding claims.

INTERNATIONAL SEARCH REPORT

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A. CLASSIFICATION OF SUBJECT MATTER
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B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 330 496 A (BEECHAM) 30 August 1989 see examples 7,6 ---	1-3,6
Y	FR 2 714 595 A (L'OREAL) 7 July 1995 see the whole document ---	1-3,6
Y	EP 0 512 814 A (UNILEVER) 11 November 1992 see examples 3,4,6,8,9 see page 7, line 21 - line 36 see page 10, line 31 - page 11, line 25 see page 3, line 49 - page 4, line 7; examples 11,12,14 ---	1-3,6
Y	EP 0 435 483 A (UNILEVER) 3 July 1991 see the whole document --- -/--	1-3,6

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

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Date of the actual completion of the international search	Date of mailing of the international search report
17 February 1997	28.02.97

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+ 31-70) 340-2040, Tx. 31 651 epo nl, Fax (+ 31-70) 340-3016	Fischer, J.P.

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 96/19302

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 86 06275 A (AVON PRODUCTS) 6 November 1986 see the whole document ---	1-6
A	WO 93 00085 A (JOHNSON & JOHNSON CONSUMER PRODUCTS) 7 January 1993 see the whole document -----	1-6

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INTERNATIONAL SEARCH REPORT

Information on patent family members

In tional Application No
PCT/US 96/19302

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
EP-A-330496	30-08-89	AU-A-	3072989	31-08-89
		DE-D-	68909970	25-11-93
		DE-T-	68909970	10-02-94
		ES-T-	2059721	16-11-94
		JP-A-	2059518	28-02-90
FR-A-2714595	07-07-95	BR-A-	9405480	19-09-95
		CA-A-	2138112	01-07-95
		EP-A-	0666076	09-08-95
		HU-A-	73060	28-06-96
		JP-A-	8000986	09-01-96
		PL-A-	306580	10-07-95
EP-A-512814	11-11-92	NONE		
EP-A-435483	03-07-91	AT-T-	113201	15-11-94
		CA-A-	2031285	08-06-91
		DE-D-	69013659	01-12-94
		DE-T-	69013659	23-03-95
		ES-T-	2063933	16-01-95
		JP-A-	4159204	02-06-92
WO-A-8606275	06-11-86	AU-A-	5772686	18-11-86
		CA-A-	1277241	04-12-90
		DE-A-	3684417	23-04-92
		EP-A-	0224504	10-06-87
		JP-T-	62502546	01-10-87
		US-A-	4826828	02-05-89
WO-A-9300085	07-01-93	AU-B-	664973	14-12-95
		AU-A-	8299791	25-01-93
		BR-A-	9106891	14-06-94
		CA-A-	2090104	28-12-92
		EG-A-	19852	31-03-96
		EP-A-	0549592	07-07-93
		JP-T-	6500079	06-01-94
		NZ-A-	239051	27-02-96
		US-A-	5559149	24-09-96
		US-A-	5583136	10-12-96